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09/993,003	11/06/2001	Richard Allen Rosenbloom	QUIG-1006US	5759

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EXAMINER	
HUI, SAN MING R	
ART UNIT	**PAPER NUMBER**
1617	10

DATE MAILED: 06/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/993,003	ROSENBLOOM, RICHARD ALLEN	
	Examiner	Art Unit	
	San-ming Hui	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the c rrespondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 March 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicant's amendments filed March 19, 2003 have been entered.

Applicant's remarks with regards to the materials printed from the internet have been considered. The Examiner has considered those materials printed from the internet.

The outstanding written description rejection under 35 USC 112, first paragraph of claims 1-11 is withdrawn in view of the Applicant's remarks filed March 19, 2003.

The outstanding rejection under 35 USC 112, second paragraph is withdrawn in view of the Applicant's remarks.

The outstanding rejections of claims 1-10 under 35 USC 103 is withdrawn in view of the applicant's remarks filed March 19, 2003. The dermatitis caused by ionized radiation such as alpha, beta, gamma, and x-ray are different in degree and in kind than that caused by UV radiation. Claim 11 is drawn to a topical composition and therefore the part addressing the method of use in the rejection under 35 USC 103 set forth in the previous office action is removed.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double

patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-11 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 and 16-20 of copending Application No. 10/132,642 and 10/045,790. Although the conflicting claims are not identical, they are not patentably distinct from each other because the differences between the instant application and the copending application is that the instant application are drawn to the method of preventing, treating or reducing radiation dermatitis caused by specific ionized radiation such as alpha radiation, beta radiation, gamma ray radiation, and x-ray radiation. One of ordinary skill in the art would reasonably expected to employ the same composition containing the same class of compound to treat or reduce radiation dermatitis broadly, because the instant composition is effective to treat or reduce radiation dermatitis caused by specific radiation.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant's remarks with regard to the filing of terminal disclaimer when the conflicting case is allowed are acknowledged.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4, and 6-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for some specific vitamin D compounds disclosed in the instant specification page 3-6, does not reasonably provide enablement for other compounds that inhibit at least one of cell differentiation and cell proliferation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. In the instant case, the instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence of absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art

7) the predictability of the art, and

8) the breadth of the claims.

Applicant fails to set forth the criteria that define "compounds that inhibits at least one of cell differentiation and cell proliferation". Additionally, Applicant fails to provide information allowing the skilled artisan to ascertain these compounds without undue experimentation. In the instant case, only a limited number of "compounds that inhibits at least one of cell differentiation and cell proliferation" examples are set forth, thereby failing to provide sufficient working examples. It is noted that these examples are neither exhaustive, nor define the class of compounds required. The pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. The instant claims read on all "compounds that inhibits at least one of cell differentiation and cell proliferation", necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. Applicants fail to provide information sufficient to practice the claimed invention, absent undue experimentation.

Response to arguments

Applicant's arguments filed March 19, 2003 averring one of skilled artisan being able to ascertain the "compounds that inhibits at least one of cell differentiation and cell proliferation" in view of the commercially available products have been considered but are not found persuasive. Examiner notes that the claims are drawn to these compounds, useful in the instant invention, not the way of screening compounds in order to find out whether the compound can inhibit cell differentiation and proliferation or not. Furthermore, applicant is attempting to use functional language in order to define the compounds by what they do, not what they are. Attention is directed to *General Electric Company v. Wabash Appliance Corporation et al* 37 USPQ 466 (US 1938), at

469, speaking to functional language at the point of novelty as herein employed: "the vice of a functional claim exists not only when a claims is "wholly" functional, if that is ever true, but when the inventor is painstaking when he recites what has already been seen, and then uses conveniently functional language at the exact point of novelty". Functional language at the point of novelty, as herein employed by Applicants, is further admonished in *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (CAFC 1997) at 1406: stating this usage does "little more than outlin[e] goals appellants hope the recited invention achieves and the problems the invention will hopefully ameliorate". Applicants functional language at the point of novelty fails to meet the requirements set forth under 35 USC 112, first paragraph. Claims employing functional language at the point of novelty, such as Applicants', neither provide those elements required to practice the inventions, nor "inform the public during the life of the patent of the limits of the monopoly asserted" *General Electric Company v. Wabash Appliance Corporation et* supra, at 468. Claims thus constructed provide no guidance as to medicaments employed, levels for providing therapeutic benefit, or provide notice for those practicing in the art, limits of protection. Simply stated, the presented claims are an invitation to experiment, not reciting a specific medicament regimen useful for practicing the instant invention.

The declaration of Dr. Richard Rosenbloom filed March 9, 2003 has been considered as to the arguments with regard to the rejections under 35 USC 112, first paragraph. The declaration merely states that there are many commercial products that can be used to screen compounds that can inhibit at least one of cell differentiation

and cell proliferation. As discussed above, it is not clear which compounds that inhibit at least one of cell differentiation and cell proliferation would be suitable for practicing the instant invention without performing undue experimentation.

New ground of rejection as to the prevention of the adverse effect of radiation dermatitis

Claim 1-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The instant claims are drawn to the prevention of one or more adverse reactions of radiation dermatitis. The specification discloses the vitamin D compounds being useful as cell proliferation inhibitors. However, the specification fails to adequately teach how to use the method to prevent one or more adverse reactions of radiation dermatitis. Radiation dermatitis is the damage of the skin that is resulted from high-energy exposure. There is only one method to prevent radiation dermatitis, and thereby the adverse reaction associated therewith, known, which is the complete blockage of the radiation (See Chapman from the Medscape Dermatology Clinic). Moreover, It is known that skin neoplasm can be caused by x-ray (See Merck Manual, page 2456, Section 247: Malignant Tumors). In other words, the claims also drawn to a method of prevent the incidence of skin cancer, which is highly unlikely due to the different factors contributing to the development of skin malignancies (See Merck Manual, page 2456, Section 247: Malignant Tumors). Thus, it is clear from the teachings of Capman that the ability to prevent one or more adverse reactions of

radiation dermatitis caused by high-energy radiation is highly unlikely and unpredictable and has met with very little success. For chronic radiation dermatitis, no treatment is even needed, according to Chapman. Applicants have not provided any convincing evidence that their claimed invention is indeed useful as preventive for one or more adverse reactions of radiation dermatitis caused by high-energy radiation and have not provided sufficient guidance to allow one skilled in the art to practice the claimed invention without undue experimentation. In the absence of such guidance and evidence, the specification fails to provide an enabling disclosure.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kita (WO97/18817, English equivalent US Patent 6,162,801), Darr et al. (British Journal of Dermatology, 1992; 127:247-253), and Sine et al. (US Patent 5,972,359) in view of Neigut (US Patent 6,048,886), Schonrock et al. (US Patent 5,876,737) and Gers-Barlag et al. (US Patent 5,952,391), references of record.

Kita teaches a vitamin D3 composition useful as skin treatment for protecting skin against the effects and damage of ultraviolet radiation (See col. 9, lines 43-48, column 10, lines 50-54). Kita also teaches the effective dosage of vitamin D3 as 0.01-100μg/ml (See col. 9, line, 8-10).

Darr et al. teaches that vitamin C or vitamin E, when administered orally or topically, is useful as treatment for ultraviolet radiation-induced damage (See Summary and page 247).

Sine et al. teaches a method of treating skin to reduce the effects of ultraviolet radiation exposure, comprising applying a composition that comprises the antioxidants, such as tocopherol acetate (vitamin E) and retinal (vitamin A), and D-panthenol, in a pharmaceutical acceptable carrier comprising acrylic copolymers, Carbopol® 954 and Carbopol® 1382 (which are known copolymers of acrylic acid and a polyallyl sucrose) which are dissolved in polyethylene glycol (See col. 3, lines 30-35, col. 39, especially Phase C: items 3 and 4, Phase D: items 4 and 9, Phase F: item 1, Phase H: item 3, lines 35-67).

The references do not expressly teach the employment of α-lipoic acid, or hydroxymethylcellulose, or one or more antioxidant enzymes, in the composition herein.

The references do not expressly teach the herein claimed amount of the actives and excipients for the composition of treating the same.

Neigut et al. teaches a composition comprising vitamin A, D, and E, α-lipoic acid, and an antioxidant enzyme, superoxide dismutasem in a corn oil vehicle for the topically treating UV radiation damage, such as dermatitis (See col. 1, lines 42-46; col. 4, lines 38-60; col. 5, lines 29-35; col. 7, Compound II, lines 40-60; col. 11, line 59 – col.13, line 60).

Schonrock et al. teaches a composition of α-tocopherol acetate and hydroxypropylmethylcellulose or hydroxymethylcellulose, useful for sunscreen and treating UV radiation induced damage (See col. 1, line 66 – col. 2, line 5, 39-44; col. 14, lines 1-44).

Gers-Barlag et al. teaches the quercetin, when topically administered, is useful in a method of treating UV radiation induced damage (See col. 1, line 6 trough col. 2, line 38; col. 14, line 25 through col. 15, line 20).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ ingredients herein claimed, in the amounts recited herein, in a topical composition.

One of ordinary skill in the art would have been motivated to employ ingredients herein claimed, in the amounts recited herein, in a topical composition. Vitamin E, superoxide dismutase, α-lipoic acid, and quercetin are known to be useful for treating radiation dermatitis. Combining these agents together useful for the same purpose is obvious (See *In re Kerkhoven* 205 USPQ 1069). Furthermore, The optimization of

result effect parameters (e.g., amounts of the actives and excipients) is obvious as being within the skill of the artisan.

Response to arguments

Applicant's arguments filed March 19, 2003 with regard to the intended use have been considered, but are not found persuasive. The intended use does not lend patentable weight to claims drawn to composition. Examiner directs attention to the Dillon ruling where the court sitting *in banc* ruled that the recitation of new utility for an old and well-known composition does not render that composition new (See *In re Dillon* 16 USPQ 2d, 1897 at 1900 (CAFC 1990)). In the instant case, the recited ingredients are all known to treat radiation dermatitis. It flows logically to combine all the recited ingredients into a single composition useful for the very same purpose, absent evidence to the contrary (See *In re Kerkhoven* 205 USPQ 1069).

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (703) 305-1002. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (703) 305-1877. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

San-ming Hui
June 2, 2003

SREENI PADMANABHAN
PRIMARY EXAMINER

6/2/03